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Sertifikaat
PATENTKANTOOR
REPUBLIC OF SOUTH AFRICA

Certificate
PATENT OFFICE
REPUBLIEK VAN SUID-AFRIKA

DEPARTEMENT VAN
HANDEL EN NYWERHEID

DEPARTMENT OF TRADE
AND INDUSTRY

19 AUG 2004

Hiermee word gesertifiseer dat
This is to certify that

REC'D 08 APR 2003
WIPO PCT

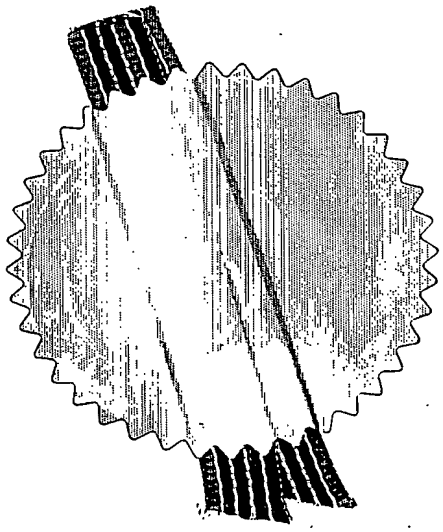
the documents attached hereto are true copies of the Forms P2, P6, provisional specification and drawings of South African Patent Application No. 2002/1395 in the name of ADCOCK INGRAM LIMITED

Filed : 19 February 2002

Entitled : PHARMACEUTICAL COMPOSITIONS

PRIORITY DOCUMENT
SUBMITTED OR TRANSMITTED IN COMPLIANCE WITH RULE 17.1(a) OR (b)

Geteken te PRETORIA in die Republiek van Suid-Afrika, hierdie **28th** dag van **February 2003**
Signed at PRETORIA in the Republic of South Africa, this **28th** day of **February 2003**



Registrateur van Patente
Registrar of Patents

FORM P.2

REPUBLIC OF SOUTH AFRICA	REGISTER OF PATENTS	PATENTS ACT, 1978

OFFICIAL APPLICATION	LODGING DATE: PROVISIONAL	ACCEPTANCE DATE
21 01 2002/ 1395	22 19 FEB 2002	47
INTERNATIONAL CLASSIFICATION	**LODGING DATE: COMPLETE**	**GRANTED DATE**
51	23	

FULL NAME(S) OF APPLICANT(S)/PATENTEE(S)

71 ADCOCK INGRAM LIMITED

APPLICANTS SUBSTITUTED: | DATE REGISTERED

71

ASSIGNEE(S) | DATE REGISTERED

71

FULL NAME(S) OF INVENTOR(S)

72 TO BE ADVISED

PRIORITY CLAIMED	COUNTRY		NUMBER		DATE	
N.B. Use International abbreviation for country (see Schedule 4)	33	NIL	31	NIL	32	NIL

TITLE OF INVENTION

54 PHARMACEUTICAL COMPOSITIONS

ADDRESS OF APPLICANT(S)/PATENTEE(S)

17 HARRISON AVENUE, BRYANSTON, GAUTENG, SOUTH AFRICA

ADDRESS FOR SERVICE	S & F REF
74 SPOOR & FISHER, SANDTON	PA132630/P

PATENT OF ADDITION NO.	DATE OF ANY CHANGE
61	
FRESH APPLICATION BASED ON	**DATE OF ANY CHANGE**

SPOOR & FISHER

REPUBLIC OF SOUTH AFRICA
PATENTS ACT, 1978

APPLICATION FOR A PATENT

AND ACKNOWLEDGEMENT OF RECEIPT
(Section 30 (1) – Regulation 22)

REPUBLIC OF SOUTH AFRICA FORM P.1
REVENUE
19.02.02 R 0060,00
HASR 505
REPUBLIEK VAN SUID AFRIKA

The granting of a patent is hereby requested by the undermentioned applicant on the basis of the present application filed in duplicate

OFFICIAL APPLICATION NO.		S & F REFERENCE
21 01	2002/1395	PA132630/P

FULL NAME(S) OF APPLICANT(S)

71	ADCOCK INGRAM LIMITED

ADDRESS(ES) OF APPLICANT(S)

	17 HARRISON AVENUE, BRYANSTON, GAUTENG, SOUTH AFRICA

TITLE OF INVENTION

54	PHARMACEUTICAL COMPOSITIONS

THE APPLICANT CLAIMS PRIORITY AS SET OUT ON THE ACCOMPANYING FORM P.2. THE EARLIEST PRIORITY CLAIM IS:

COUNTRY:	NUMBER:	DATE:
NIL	NIL	NIL

~~THIS APPLICATION IS FOR A PATENT OF ADDITION TO PATENT APPLICATION NO.~~

21	01	

~~THIS APPLICATION IS A FRESH APPLICATION IN TERMS OF SECTION 37 AND IS BASED ON APPLICATION NO.~~

21	01	

THIS APPLICATION IS ACCOMPANIED BY:

- [x] 1. A single copy of a provisional specification of 5 pages.
- [ ] 2. Drawings of sheets
- [ ] 3. Publication particulars and abstract (Form P.8 in duplicate).
- [ ] 4. A copy of Figure of the drawings (if any) for the abstract.
- [ ] 5. Assignment of invention.
- [ ] 6. Certified priority document.
- [ ] 7. Translation of the priority document.
- [ ] 8. Assignment of priority rights.
- [ ] 9. A copy of the Form P.2 and the specification of S.A. Patent Application No .
- [ ] 10. Declaration and power of attorney on Form P.3.
- [ ] 11. Request for ante-dating on Form P.4.
- [ ] 12. Request for classification on Form P.9.
- [x] 13. Form P.2 in duplicate.
- [ ] 14. Other.

74	ADDRESS FOR SERVICE: SPOOR & FISHER, SANDTON

Dated: 19 February 2002

SPOOR & FISHER
PATENT ATTORNEYS FOR THE APPLICANT(S)

RECEIVED
REGISTRAR OF PATENTS DESIGNS, TRADE MARKS AND COPYRIGHT
2002 -02- 19
REGISTRATEUR VAN PATENTE, MODELLE, HANDELSMERKE EN OUTEURSREG
REGISTRAR OF PATENTS

SPOOR & FISHER

FORM P.6

REPUBLIC OF SOUTH AFRICA
PATENTS ACT, 1978

PROVISIONAL SPECIFICATION

(Section 30(1) – Regulation 27)

OFFICIAL APPLICATION NO.		LODGING DATE	
21 01	2002/1395	22	19 FEBRUARY 2002

FULL NAMES OF APPLICANTS

71	ADCOCK INGRAM LIMITED

FULL NAMES OF INVENTOR

72	TO BE ADVISED

TITLE OF INVENTION

54	PHARMACEUTICAL COMPOSITIONS

BACKGROUND OF THE INVENTION

This invention relates to pharmaceutical compositions and their use in the symptomatic relief and treatment of pain, with or without fever.

SUMMARY OF THE INVENTION

According to one aspect of the invention, a pharmaceutical composition comprises a combination of (i) an analgesic, (ii) a selective or specific COX-2 inhibitor, and (iii) an opiate, and a pharmaceutically acceptable carrier.

In a preferred composition of the invention the analgesic (i) is paracetamol or a pharmaceutically acceptable salt or derivative thereof, the selective or specific COX-2 inhibitor (ii) is selected from the group comprising meloxicam, celecoxib, rofecoxib and pharmaceutically acceptable salts or derivatives thereof, and the opiate (iii) is selected from the group

comprising codeine, morphine, tramadol, fentanyl and pharmaceutically acceptable salts or derivatives thereof.

A particularly preferred composition of the invention comprises a combination of paracetamol, meloxicam and codeine phosphate.

The invention extends to the use of a pharmaceutical composition as defined above in a method of providing symptomatic relief or treatment of pain, with or without fever, in particular that associated with inflammation such as that associated with trauma, osteoarthritis or rheumatoid arthritis, for example.

The invention also extends to the use of a combination of (i), (ii) and (iii) in the manufacture of a medicament for use in the symptomatic relief or treatment of pain, with or without fever.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

The pharmaceutical compositions of the invention are suitable for the symptomatic relief or treatment of pain with or without fever, in particular but not limited to that associated with inflammatory processes, such as trauma, osteoarthritis or rheumatoid arthritis, for example.

The first ingredient is an analgesic such as paracetamol (acetaminophen) or a pharmaceutically acceptable salt or derivative thereof. It has analgesic and antipyretic properties but limited or no anti-inflammatory action.

The daily dose of the paracetamol active ingredient is typically in the range of about 60 mg (children) to about 4000 mg (adults).

The second ingredient is a selective or specific COX-2 inhibitor such as meloxicam, celecoxib and rofecoxib, for example. These agents have anti-inflammatory and analgesic properties. Their ability to inhibit the action of COX-2 and not COX-1 has been shown to provide an enhanced safety profile for these compounds when compared to non-specific COX inhibitors.

In the case of meloxicam as active ingredient, the daily dose is typically in the range of about 3.75 mg to about 30 mg, preferably about 7.5 mg to about 15 mg.

The third ingredient is an opiate such as codeine, morphine, tramadol or fentanyl, for example. These compounds bind with specific receptors at many sites within the central nervous system to alter processes affecting both the perception of pain and the emotional response to pain.

The daily dose of the opiate, in the case of codeine phosphate, is 10 mg to 360 mg.

A pharmaceutical composition comprising a combination of an analgesic, an opiate and a selective or specific COX-2 inhibitor includes a pharmaceutically acceptable carrier and may include other necessary non-active excipients such as, for example, sorbitol, sucrose, saccharin, starch, lactose, guar gum, xanthan gum, magnesium stearate, bees wax, talc, methylcellulose, dextrin or povidone. The pharmaceutical composition may be provided in any appropriate dosage form such as, for example, tablets, capsules, granules, suspensions, solutions or other liquid forms, and is intended for oral, rectal or intravenous administration.

The dosage form will typically be administered to a patient from 2 to 4 times per day.

Although the active ingredients would typically be administered at currently accepted therapeutic doses, it is envisaged that one or more actives could be administered at lower than currently recognized doses while still providing effective pain relief/treatment.

DATED THIS 19th DAY OF FEBRUARY 2002

SPOOR & FISHER
APPLICANT'S PATENT ATTORNEYS